## REMARKS

In view of the amendments and remarks herein, the Examiner is requested to allow Claims 1, 3-4, 8-14, 16-19, 21-24, 35, 37 and 39, the only claims pending and under examination in this application.

Claims 1, 11 and 24 have been amended to incorporate the elements of Claims 34, 36 and 38, respectively, which have been correspondingly cancelled.

In addition, Claim 1 has been amended to incorporate the elements of Claim 2, which has been correspondingly cancelled, and Claim 11 has been amended to incorporate the elements of Claim 15, which has been correspondingly cancelled. Also, Claim 24 has been amended to include the element that "at least two features on said chemical array are of different sizes." Further support for these amendments can be found in the specification in paragraph [0006], starting on page 1.

Claims 3 and 4, which formerly depended from Claim 2 (now cancelled), have been amended to depend from Claim 1. Similarly, Claims 16 and 17, which formerly depended from Claim 15 (now cancelled), have been amended to depend from Claim 11.

As no new matter has been added by way of the above amendments, entry thereof by the Examiner is respectfully requested.

### *Claim Objections*

Claims 34, 36 and 38 were objected to under 37 C.F.R. § 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. As indicated above, Claims 1, 11 and 24 have been amended to incorporate the elements of Claims 34, 36 and 38, respectively. Claims 34, 36 and 38 have been correspondingly cancelled, rendering this objection moot. The Applicants respectfully request withdrawal of this objection.

***Claim Rejections – 35 U.S.C. § 103***

Claims 1-4, 8-19, 21-24 and 34-39 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Webb et al. (GB 2355716) in view of Blanchard (U.S. Patent No. 6,419,883).

In order to meet its burden in establishing a rejection under 35 U.S.C. §103, the Office must first demonstrate that a prior art reference, or references when combined, teach or suggest all claim elements. *See e.g., KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007); *Pharmastem Therapeutics v. Viacell et al.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007); MPEP § 2143(A)(1). In addition to demonstrating that all the elements were known in the prior art, the Office must also articulate a reason for combining the elements. *See e.g., KSR*, 127 S.Ct. at 1741; *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 243 Fed. Appx. 592, 595-596 (Fed. Cir. 2007) (citing *KSR*). Further, the Supreme Court in *KSR* also stated that that "a court *must* ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR*, 127 S.Ct. at 1740 (emphasis added). As such, in addition to showing that all elements of a claim were known in the prior art and that one of skill had a reason to combine them, the Office must also provide evidence that the combination would be a predicted success.

The rejected claims are directed to methods of fabricating a chemical array of biopolymeric ligands and include the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition". In addition, as currently amended, Claims 1 and 24 include the element that at least two features on the chemical array are of different sizes, and Claim 11 includes the element that the feature size of a first feature on the chemical array is different than the feature size of a second feature on the chemical array.

In maintaining the current rejection, the Examiner alleges that "Webb specifically teaches chemical layout (i.e. target drive pattern) which includes the 'instructions for driving the apparatus components as required to form the target

array (which includes target locations and dimensions for each spot)'". Office Action, pg. 6, lines 19-22 (citing Webb, paragraph spanning pages 30-31).

The Applicants respectfully disagree. Webb actually discloses that "the operation is basically [as] follows: (i) determine (402) target drive pattern (if not already provided) to obtain target array pattern, based on nominal operating parameters and target polynucleotide array pattern". Webb, pg. 31, lines 16-22. Thus, Webb disclose that the target array pattern is based on nominal operating parameters. In addition, Webb discloses as follows:

> The at least one operating parameter can be selected from one or more of any parameter which would affect the actual array pattern deposited. For example, these may include: a position of the dispensing head or any other dispensing apparatus component; the accuracy of an encoder used to detect the position of the dispensing head or the substrate; the accuracy in an ability of the transport system to move the substrate or head to an expected location in response to a command (for example, deviation of actual movement from a corresponding nominal axis of movement); or the position of a position of a nozzle in a multiple nozzle dispensing head.

Webb, pg. 9, lines 15-23.

In contrast, the present disclosure states as follows:

> Embodiments of the subject invention enable a chemical array to be prepared or "customized" at least with respect to each feature size of the prepared array. This customization may be accomplished by determining a chemical array layout in which each feature in the chemical array layout has a size that is chosen based on its composition, and fabricating a chemical array according to the biopolymeric array layout. As described in greater detail below, one manner in which this may be accomplished is by providing various activation signals to different ejectors of a fluid drop deposition device employed to fabricate the array according to the array layout. In other words, precisely controlling the particular activation signal provided to each ejector of a deposition head enables customization of the size of each feature of an array. As the activation signal provided to an ejector is directly related to the amount of fluid ejected from an orifice associated with that particular orifice, ejectors capable of being activated using differing signals to eject different amounts of fluids therefrom provides precise control over the

> feature sizes of an array is provided and thus enable fabrication of an array of features of various sizes.

Specification, pg. 13-14, ¶ [0065].

Furthermore, the present disclosure states that, "the ability to control the size of each feature of an array is provided by the subject methods. That is, the subject methods provide the ability to customize the chemistry or feature size for each feature (e.g., for each synthesized base) on a per surface bound ligand, e.g., probe, basis (as opposed to a per print swath column or per entire substrate or entire substrate layer basis)." Specification, pg. 14-15, ¶ [0067].

However, nowhere does Webb disclose or suggest the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition", as required by the instant claims.

In addition, Webb does not disclose or suggest chemical arrays that include at least two features of different sizes. Webb actually discloses that "if there is an error in one or more operating parameters (406) then processor 140 derives, based on the error, a corrected drive pattern from the target pattern such that use of the corrected drive pattern results in a reduced discrepancy between the target and actual array patterns than would have occurred is the target drive pattern had been used." Webb, pg. 31, lines 24-28. As such, Webb discloses identifying errors in feature sizes and correcting those errors. See Webb, pg. 34, line 1 to pg. 35, line 3, and FIGS. 16-19. Consequently, Webb fails to disclose or suggest chemical arrays that include at least two features of different sizes.

Furthermore, the Applicants contend that nowhere does Blanchard disclose or suggest chemical arrays that include at least two features of different sizes.

The Examiner concedes that "Blanchard differs from the claimed invention in that the reference does not specifically teach modulating the deposition head to dispense differing volumes to thereby produce the differing sized features." Office

Action, pg. 7, lines 17-19. Moreover, Blanchard discloses that "the amount of solute, e.g., a reactive chemical species, that is to be dispensed as a microdroplet solution, should preferably be uniform from microdroplet to microdroplet", and that "This property is particularly important when the dispensed microdroplets are to be deposited in closely packed arrays of uniformly shaped microdots that cannot overlap." Blanchard, col. 7, lines 22-26 and lines 37-40. Thus, Blanchard discloses that "microdroplets are to be deposited in closely packed arrays of uniformly shaped microdots". As such, Blanchard does not disclose or suggest the Applicants' claimed element that "at least two features on said chemical array are of different sizes", and in fact teaches away from this element.

In addition, Blanchard actually discloses that "surface tension wells can constrain each microdot, and prevent adjacent microdots from overlapping or merging with each other. According to the invention, methods have been developed that produce an array of microdots that are in the form of circular wells." Blanchard, col. 9, lines 37-42. See also FIG. 1a of Blanchard, reproduced below:

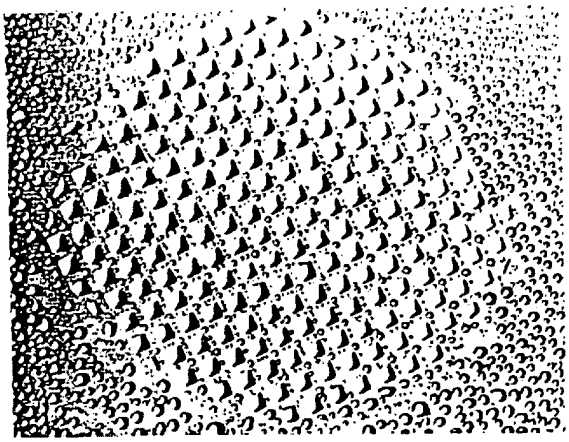

Fig. 1a

Thus, in light of the above, Blanchard is not teaching spots of different sizes *on a single array*, as suggested by the Examiner, but rather that different arrays may have different sized spots. In other words, each array has a uniform spot size, but when compared to other arrays, each array may have different size spots from

another. Consequently, Blanchard fails to disclose or suggest the Applicants' claimed element that "at least two features on said chemical array are of different sizes."

The Examiner further alleges that, "Blanchard teaches layout determination". Office Action, pg. 7, lines 3 (citing Blanchard, col. 34, lines 1-4).

The Applicants respectfully disagree. Blanchard merely discloses that, "The program then read in a list containing the name of an oligo specification file storing the geometry of the desired pattern to be deposited in a particular wafer to be processed in a particular run". Blanchard, col. 34, lines 1-4. Blanchard further discloses that, "The program then calculates all trigger RAM **201** entries that will be used, which include a distinct inkjet nozzle trigger point (X-location) and a distinct column of dots in the pattern on a wafer at each trigger point (step **1009**). The program then calculates all Y-positions (passes) that the scanning arm will need to make . . . The required Y-positions are determined by the number and spacing of the rows of dots in the desired pattern and the space spanned by a column of inkjet nozzles on an inkjet head." Blanchard, col. 34, lines 9-20.

As such, Blanchard fails to disclose or suggest the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition", as required by the instant claims. Thus, Blanchard fails to remedy the deficiencies in Webb.

Consequently, the cited combination of Webb and Blanchard fails to disclose or suggest all the elements of the Applicants' claimed invention. The Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1-4, 8-19, 21-24 and 34-39 be withdrawn.

Claims 1-4, 8-19, 21-24 and 34-39 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Blanchard (U.S. Patent No. 6,419,883) in view of Hirota et al. (U.S. Patent No. 6,753,144).

As indicated above, the rejected claims are directed to methods of fabricating a chemical array of biopolymeric ligands and include the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition".

In maintaining the instant rejection, the Examiner asserts that, "Hirota provides the element missing from Blanchard i.e. waveform modulation to produce different volumes and different spot sizes. And Blanchard provides the elements missing from Hirota i.e. array layout, computer controlled deposition and phosphoramidite." Office Action, pg. 15, lines 10-13.

The Applicants respectfully disagree. As stated by the Examiner above, Blanchard is deficient in that it fails to teach waveform modulation to produce different volumes and different spot sizes. In addition, as stated by the Examiner, Hirota is deficient in that it fails to teach array layout, computer controlled deposition and phosphoramidite.

As discussed above, Blanchard is also deficient in that Blanchard fails to disclose or suggest the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition", as required by the instant claims. In contrast, Blanchard merely discloses that, "The required Y-positions are determined by the number and spacing of the rows of dots in the desired pattern and the space spanned by a column of inkjet nozzles on an inkjet head." Blanchard, col. 34, lines 9-20. Nowhere does Blanchard disclose or suggest that each feature in the chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition, as claimed by the Applicants.

Consequently, both Blanchard and Hirota fail to disclose or suggest the claimed element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its

biopolymeric ligand composition". For this reason alone, this rejection may be withdrawn.

Additionally, the rejected claims include the element that "at least one of the fluids dispensed from said fluid drop deposition device is a phosphoramidite fluid, and wherein said method is a method for *in situ* fabrication of said chemical array of biopolymeric ligands." This *in situ* method is captured in the claims, for example in the elements that: "each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition"; "said fabricating comprises modulating an applied activation signal for each ejector of said at least one deposition head to produce said features"; and 'said method further comprises transmitting said feature sizes to said processor, whereby said processor performs said modulating based on said feature sizes". In addition, the Applicants' specification further discloses that "the ability to control the size of each feature of an array is provided by the subject methods. That is, the subject methods provide the ability to customize the chemistry or feature size for each feature (e.g., for each synthesized base) on a per surface bound ligand, e.g., probe, basis (as opposed to a per print swath column or per entire substrate or entire substrate layer basis)." Specification, pg. 15-16, ¶ [0067].

The Examiner concedes that Blanchard "does not specifically teach modulating the deposition head to dispense differing volumes to thereby produce the differing sized features." Office Action, pg. 7, lines 17-19. As such, Blanchard fails to disclose or suggest a method for *in situ* array fabrication, as claimed by the Applicants.

In addition, Hirota also fails to disclose or suggest a method for *in situ* array fabrication. Hirota actually discloses that producing a DNA microarray includes "a sample preparation step **S2** of preparing the sample solution containing DNA fragment, and a supply step **S3** of supplying the obtained sample solution onto the base plate **10**." Hirota, col. 6, lines 43-46, and Figs. 2-3. In addition, Hirota discloses that the DNA fragments are "PCR product[s] amplified by using a known PCR machine". Hirota, col. 7, lines 8-10. Thus, Hirota only discloses producing a

DNA microarray by affixing DNA fragments obtained by PCR onto a base plate, and in no way discloses or suggests a method for *in situ* array fabrication, as claimed by the Applicants. Consequently, nowhere does Blanchard or Hirota disclose or suggest the Applicants' claimed method of *in situ* array fabrication.

Furthermore, as discussed above, nowhere does Blanchard disclose or suggest chemical arrays with at least two features of different sizes. The Applicants submit that Hirota also fails to disclose or suggest this element. In describing methods of producing a DNA microarray, Hirota actually discloses as follows:

> During this process, when the supply position is appropriately changed, the droplets of the supplied sample solution are combined (integrated) on the base plate **10** to form the sample solution having one spot diameter. Further, it is possible to realize a uniform spot diameter formed on the base plate **10** by controlling the number of supply operations, the supply position, and the amount of one time supply, depending on the type of the sample solution to be supplied.

Hirota, col. 12, lines 36-44.

Thus, Hirota discloses that the droplets on the base plate have "a uniform spot diameter". Consequently, similar to Blanchard discussed above, Hirota does not disclose or suggest chemical arrays with at least two features of different sizes, as claimed by the Applicants.

In view of the above, a *prima facie* case of obviousness cannot be maintained because the cited combination of Blanchard and Hirota fails to teach or suggest all the elements of the rejected claims. Consequently, the Applicants respectfully request that the rejection of Claims 1-4, 8-19, 21-24 and 34-39 under 35 U.S.C. § 103(a) be withdrawn.

## CONCLUSION

In view of the amendments and remarks above, Applicant(s) respectfully submit(s) that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret E. Field, (650) 327-3400.

The Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078, order number 10031095-1.

Respectfully submitted,

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